PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
02012302.2		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP 03/05780	03.06.2003	04.06.2002
International Patent Classification (IPC) or both national classification and IPC		
C12N15/29		
Applicant		
BIOMAY PRODUKTIONS- UND HANDELS-AKTIENGESELLSCHAFT		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 3 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
17.11.2003	14.09.2004
Name and mailing address of the international preliminary examining authority:	Authorized Officer
European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Bucka, A Telephone No. +31 70 340-2279

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/05780

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-28 as originally filed

Sequence listings part of the description, Pages

1-5 as originally filed

Claims, Numbers

1-18 received on 27.08.2004 with letter of 27.08.2004

Drawings, Sheets

1/10-10/10 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☒ contained in the international application in written form.

   ☒ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-18
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-18
Industrial applicability (IA)	Yes:	Claims	1-18
	No:	Claims	

2. Citations and explanations

   see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1 The following documents (D) are considered to be relevant to this application:

D1: WO 96 13589 A (IMMULOGIC PHARMA CORP) 9 May 1996

D2: WO 94 01560 A (IMMULOGIC PHARMA CORP ;BOND JULIAN F (US); KUO MEI CHANG (US); POL) 20 January 1994

D3: FERREIRA FATIMA ET AL: 'Isolation and characterization of cDNA clones coding for mugwort (Artemisia vulgaris) pollen allergens.' INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, vol. **124**, no. 1-3, January 2001, pages 77-79.

D4: HIRSCHWEHR R ET AL: 'ALLERGENS, IGE, MEDIATORS, INFLAMMATORY MECHANISMS. IDENTIFICATION OF COMMON ALLERGENIC STRUCTURES IN MUGWORT AND RAGWEED POLLEN' JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, MOSBY - YEARLY BOOK, INC, US, vol. **101**, no. 2, February 1998, pages 196-206.

2 The amendments of the claims submitted with letter of 27 August 2004 appear to be allowable in view of Article 34(2)(b) PCT.

3 The subject-matter of **claims 1 to 18** is new and therefore meets the requirements of Article 33(2) PCT.

4 The subject-matter of **claims 1 to 18** lacks inventiveness in the meaning of Article 33(3) PCT.

Claim 1 relates to an allergen from mugwort having the sequence as shown in SEQ ID NO: 1, which shows homology to an allergen from ragweed.

D3, which is considered to represent the closest prior art, describes the identification of several cDNAs encoding mugwort pollen allergens, from which the subject-matter of claim 1 differs in that the primary sequence of the antigen is different from those contained in the prior art.

The problem to be solved by the present invention therefore is considered to be the provision of a further or alternative mugwort pollen allergen.

The application provides the protein having the sequence SEQ ID NO: 1, thereby solving the problem.

D3 is referring to the same technical problem, namely the identification of mugwort antigens. In view of the teachings of D4, describing *inter alia* the cross-reactivity of antisera against ragweed allergens with allergens from mugwort, and in view of the availability of the cDNA expression library described in D3, the identification of the provided cDNA would have been straightforward to a person skilled in the art.

D4 describes the cross-reactivity both of IgE antibodies and of rabbit antisera against the antigen profilin (figures 3 to 5). Therefore, the skilled person would have a reasonable expectation to succeed in the identification of related antigens from a different species, since the cross-reactivity of antibodies has been demonstrated in D4. D4 even teaches two approaches, which lead to the isolation of related antigens. Therefore, even if it would require much work, i. e. the use of both approaches, the skilled person would have the reasonable expectation to succeed in the identification of further, related antigens from mugwort. It is common to both approaches that the crossreactivity of antibodies is used to identify antigens from two different, related species. This is exactly the reasoning used in the application at issue for the isolation of a cDNA encoding a mugwort allergen.

The Applicant states that difficulties were encountered in the cloning of the antigen that required inventive activity to be overcome, and also that the skilled person "can in no way simply receive the specific sera required for the identification of a new antigen". However, the application does not describe any such cloning difficulties that would have required inventiveness to be overcome. Even more strikingly, the antisera used in the identification of the new antigen, was, according to the application, simply obtained from Dr. P. King. The antiserum in question was a rabbit antiserum (IgG) highly specific for *ragweed* pollen (page 15).

Therefore, the skilled artisan can expect to perform the cloning and expression of the corresponding cDNA in a fairly uncomplicated manner, even if this would require much work.

For the reasons outlined above, the solution proposed in **claims 1 to 18** cannot be considered as involving an inventive step (Article 33(3) PCT).

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Claims

1. A polypeptide selected from the group consisting of:

   a) polypeptides comprising a fragment of at least 18 consecutive amino acids of the amino acid sequence as shown in SEQ ID NO:1;

   b) polypeptides comprising an amino acid sequence which has an identity of at least 70% to the amino acid sequence as shown in SEQ ID NO:1; and

   c) polypeptides consisting of at least 8 contiguous amino acids of the amino acid sequence as shown in SEQ ID NO:1.

2. A polypeptide according to claim 1, comprising a fragment of the amino acid sequence as shown in SEQ ID NO:1 wherein said fragment is capable of binding to IgE antibodies from an individual being allergic against mugwort pollen.

3. A polypeptide according to claim 1 or 2, comprising the amino acid sequence as shown in SEQ ID NO:1.

4. A polypeptide according to any one of claims 1 to 3, characterized in that it is capable of binding to IgE antibodies from an individual being allergic against ragweed pollen.

5. A polynucleotide selected from the group consisting of

   a) polynucleotides encoding the amino acid sequence as shown in SEQ ID NO:1;

   b) polynucleotides encoding a polypeptide as claimed in any one of claims 1 to 4; and

c) polynucleotides comprising a nucleotide sequence which has an identity of at least 75 % to the nucleotide sequence as shown in SEQ ID NO:2;

or the complementary strand of such polynucleotide.

6. A polynucleotide according to claim 5 comprising the nucleotide sequence as shown in SEQ ID NO:2 or the nucleotide sequence as shown in SEQ ID NO:3.

7. A plasmid or a vector comprising a polynucleotide as claimed in claim 5 or 6.

8. A cell containing a plasmid or a vector as claimed in claim 7 and/or a polynucleotide as claimed in claim 5 or 6.

9. A cell according to claim 8 which is selected from the group consisting of plant cells, bacterial cells and yeast cells.

10. A process for the preparation of a polypeptide as claimed in any one of claims 1 to 4 comprising the step of culturing cells as claimed in claim 8 or 9 under conditions appropriate for the expression of the polypeptide and optionally subsequently recovering the polypeptide.

11. A process according to claim 10 wherein the cells are opened and the polypeptide is recovered using affinity chromatography.

12. An antibody capable of binding to a polypeptide as claimed in any one of claims 1 to 4.

13. An antibody according to claim 12 which is capable of binding to one or several of the polypeptides selected from the group consisting of Amb a I.1, Amb a I.2, Amb a I.3 and Amb a 2.

14. An antibody according to claim 12 which does not bind to any one of the polypeptides selected from the group consisting of Amb a I.1, Amb a I.2, Amb a I.3 and Amb a 2.

15. A pharmaceutical composition comprising a polypeptide as claimed in any one of claims 1 to 4 and/or a polynucleotide as claimed in claim 5 or 6 and/or an antibody as claimed in any one of claims 12 to 14.

16. The use of a polypeptide as claimed in any one of claims 1 to 4 or a polynucleotide as claimed in claim 5 or 6 or an antibody as claimed in any one of claims 12 to 14 for the preparation of a medicament for the treatment or the prevention or the diagnosis of an allergic disorder.

17. A use according to claim 16 wherein the medicament is administered to an individual to be desensitized.

18. A kit useful for the diagnosis, the treatment and/or the prevention of an allergic disorder comprising a polypeptide as claimed in any one of claims 1 to 4 and/or a polynucleotide as claimed in claim 5 or 6 and/or an antibody as claimed in any one of claims 12 to 14.